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Geographic Variation in the Association between Ambient Fine Particulate Matter ($PM_{2.5}$) and Term Low Birth Weight in the United States

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Abstract

Background: Studies on the association between prenatal exposure to fine particulate matter with ≤ 2.5 micrometers in aerodynamic diameter ($PM_{2.5}$) and term low birth weight (LBW) have resulted in inconsistent findings. Most studies were conducted in snapshots of small geographic areas and no national study exists.

Objectives: We investigated geographic variation in the associations between ambient $PM_{2.5}$ during pregnancy and term LBW in the contiguous United States (US).

Methods: 3,389,450 term singleton births in 2002 (37 – 44 weeks gestational age and birth weight of 1,000g – 5,500g) were linked to daily $PM_{2.5}$ via imputed birth days. We generated average daily $PM_{2.5}$ during the entire pregnancy and each trimester. Multilevel logistic regression models with county-level random effects were used to evaluate the associations between term LBW and $PM_{2.5}$ during pregnancy.

Results: Without adjusting for covariates, the odds of term LBW increased 2% (OR=1.02; 95% CI: 1.00, 1.03) for every 5 μg/m³ increase in $PM_{2.5}$ exposure during the second trimester only, which remained unchanged after adjusting for county-level poverty (OR=1.02; 95% CI: 1.01, 1.04). The odds did change to null after adjusting for individual-level predictors (OR=1.00; 95% CI: 0.99, 1.02). Multilevel analyses, stratified by census division, revealed significant positive associations of term LBW and $PM_{2.5}$ exposure (during the entire pregnancy or a specific trimester) in three census divisions: Middle Atlantic, East North Central, and West North Central, and significant negative association in the Mountain division.

Conclusions: Our study provided additional evidence on the associations between $PM_{2.5}$ exposure during pregnancy and term LBW from a national perspective. The magnitude and direction of the estimated associations between $PM_{2.5}$ exposure and term LBW varied by geographic locations in the US.

Introduction

Low birth weight (LBW) is a known risk factor for infant morbidity and mortality and chronic health problems in later life (McCormick 1985). Maternal exposure to particulate matter ($PM_{2.5}$– fine particulate matter with aerodynamic diameter ≤2.5μm and PM_{10} – particulate matter with aerodynamic diameter ≤10μm) during pregnancy may contribute to adverse reproductive health outcomes including term LBW (Backes et al. 2013; Dadvand et al. 2013; Fleischer et al. 2014; Pedersen et al. 2013; Sapkota et al. 2012; Stieb et al. 2012). Findings from studies of associations between prenatal exposure to $PM_{2.5}$ and PM_{10} and adverse reproductive health outcomes have been inconsistent (Bosetti et al. 2010; Sapkota et al. 2012; Shah and Balkhair 2011; Stieb et al. 2012). For instance, PM_{10} and $PM_{2.5}$ were found to be associated with term LBW in Connecticut and Massachusetts (Bell et al. 2007b), California and six northeastern cities ($PM_{2.5}$) (Maisonet et al. 2001; Parker et al. 2005), Allegheny County, PA (PM_{10}) (Xu et al. 2011), United States (US); Europe ($PM_{2.5}$) (Pedersen et al. 2013), Sao Paulo, Brazil (PM_{10}) (Gouveia et al. 2004); and Seoul, Korea (PM_{10}) (Lee et al. 2003); however, no such evidence reported in Seattle, WA, US ($PM_{2.5}$) (Dadvand et al. 2013); Oslo, Norway (Madsen et al. 2010); and The Netherlands (Gehring et al. 2011; Pedersen et al. 2013); and mixed evidences exist in a few systematic reviews and meta analyses (Sapkota et al. 2012; Shah and Balkhair 2011; Stieb et al. 2012). Heterogeneity in the published findings may arise from differences in many aspects of the study designs and available data. For example, the methods of assigning exposure may vary, given that the consistent and high quality air pollution exposure data were rarely available across large geographic areas in the past.

Most published studies have concerned limited geographic areas or time periods, often with small sample size, in part due to sparsely distributed air pollution monitoring data. A few studies with larger geographic coverage have reported geographic variation in associations between air pollution and LBW. A study of term singleton births from 397 counties in the US showed that the associations between $PM_{2.5}$ and term LBW varied greatly by region (Parker and Woodruff 2008). A recent international collaboration reexamined data from multiple countries using a standard protocol and confirmed the existence of geographical variation in associations between $PM_{2.5}$ and LBW (Dadvand et al. 2013). To our best knowledge, no national study in the US has previously linked daily $PM_{2.5}$ with birth gestational ages of pregnancies and examined the associations between $PM_{2.5}$ exposure during pregnancy and term LBW. In this study, we linked 2001 – 2002 daily $PM_{2.5}$ estimates with all term singleton births (3,389,450) in 2002 in all 3,109 counties in the contiguous US and explored geographic variation in the associations between ambient $PM_{2.5}$ exposure and term LBW via a multilevel approach. We limited our study area to the contiguous US (48 states and District of Columbia), because $PM_{2.5}$ data are not available in the non-contiguous states of Alaska and Hawaii.

Methods

Study population

Birth data used in this study were obtained from the National Environmental Public Health Tracking Network (Tracking Network) (Centers for Disease Control and Prevention 2013). The Tracking Network is a system of integrated health, exposure, and hazard information and data from a variety of national, state, and city sources. Birth data on the Tracking Network were

obtained from the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC) (Martin et al. 2007). We included all singletons with gestational age of 37 – 44 weeks and birth weight of 1,000g – 5,500g (3,389,450 term births) born to mothers who resided in the contiguous US in 2002. The US birth certificate system underwent a revision starting 2003 which states have implemented in a piecemeal manner over the years (ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/DVS/natality). To avoid the data coding inconsistency problems associated with birth certificate revision, we decided to use 2002 birth data only. We excluded those births with missing values of race/ethnicity (18,215, less than 1%), parity (6,960, less than 1%), maternal education (41,098, 1%), and prenatal care utilization (55,663, 2%). We further excluded all births with missing data for smoking status (14,036, less than 1%) with the exception of California births, since smoking status were not recorded in California birth certificates in 2002 and an unknown category of smoking status was assigned for all California births. Our final analytical dataset included 3,271,203 (96.5%) term births.

$PM_{2.5}$ exposure assignment

The 2001–2002 daily census tract-level $PM_{2.5}$ concentration data for the contiguous US were generated by the U.S. Environmental Protection Agency for the Tracking Network using Hierarchical Bayesian models based on data from the Community Multi-scale Air Quality modeling system, including emission, meteorology, and chemical modeling components, and air monitoring stations (McMillan et al. 2010; U.S. Environmental Protection Agency 2010). Census tract is the geographic unit nested to county and is often used as a geographic proxy for local community. On average, a census tract contains about 4,300 inhabitants, ranging 0 from to

36,146 in 2000. We aggregated census-tract-level daily $PM_{2.5}$ estimates and weighted by 2000 census tract populations to generate county-level daily $PM_{2.5}$ estimates for 3,109 counties (average 89,927 inhabitants, ranging from 67 to 9,519,338 in 2000) in the contiguous US.

We linked birth data and daily $PM_{2.5}$ estimates by both county identifiers and pregnancy dates from conception to birth. The start and end date of pregnancy or trimester were determined by infant birth date and gestational age (only available in completed weeks) at birth. Since only birth month, instead of birth date, was accessible to researchers due to confidentiality, we imputed birth day as the random day within the birth month via a uniform distribution, which means any day within the birth month could be a birth day with equal probability. Individualized $PM_{2.5}$ exposure of a term birth was summarized as county-level average daily $PM_{2.5}$ concentration during the entire pregnancy and each trimester (first trimester: weeks 1 – 13, second trimester 2: weeks 14 – 26, and third trimester: weeks 27 – birth or 44 weeks) based on the maternal county of residence listed on the birth certificate. Thus, each birth had $PM_{2.5}$ exposure estimates for the entire pregnancy, and for the first, second and third trimesters.

Main outcome and covariates

Our outcome variable was term LBW (1,000 g < weight < 2500 g), versus normal birth weight (2,500 g ≤ weight < 5,500 g). Individual-level predictors included average daily $PM_{2.5}$ as well as infant and maternal demographics. Average daily $PM_{2.5}$ during the entire pregnancy and each trimester for each birth was treated as a continuous predictor. All other predictors were categorical: infant gender (female versus male), parity (first live birth versus non-first live birth), gestational age (37, 38, 39, and 40–44 weeks), maternal age(<20, 20–34, and 35+ years),

maternal race/ethnicity (Hispanic, non-Hispanic white, Black, and other races), marital status (not married versus married), educational attainment (<12, 12, 13–15, and 16+ years), prenatal care start time (fourth month or later/no care versus first–third month), smoking (smoker, non-smoker), birth season (Spring (March–May), Summer (June–August), Fall (September–November), and Winter (December–February); and nine US census divisions (New England, Middle Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain, Pacific) (U.S. Census Bureau 2005).

Our county-level socioeconomic status (SES) predictor was poverty, measured as the percentage of county residents below the federal poverty line. Prior studies reveal that this measure is superior to other area-based measures of SES (e.g., median home value) in sensitivity to SES-related health outcomes (Krieger 2007). We obtained 2002 county poverty data from US Census' Small Area Income and Poverty Estimates program (U.S. Census Bureau 2013) and linked them with birth data. Counties were categorized into four groups according to their poverty rates: < 10%, 10%–14.9%, 15%–19.9%, and ≥ 20%.

Statistical Analysis

We used multilevel logistic regression models with county-level random effects to examine the associations of $PM_{2.5}$ exposure during pregnancy and term LBW. The odds ratio (OR) or adjusted odds ratio (AOR) was used to measure associations. The p-value of less than 0.05 was used to define statistical significance of associations.

First, we conducted the main analyses using full study population with four different $PM_{2.5}$ exposure estimates: entire pregnancy, first trimester, second trimester, and third trimester. A

series of models were constructed for each of four $PM_{2.5}$ exposure estimates during pregnancy and three of them were presented: Model 1 included only $PM_{2.5}$ exposure and county-level random effects, Model 2 was Model 1 plus county poverty, and Model 3 was Model 2 plus all individual predictors, including infant's gender and parity, gestational age, mother's age, race/ethnicity, marital status, education, prenatal care, birth season, and census division. We presented AORs (OR for Model 1) and confidence intervals (CIs) for independent variables while accounting for potential within-county correlations among term births from the same counties via county-level random effects.

Second, we conducted stratified analyses by U.S. census division to explore the associations between term LBW and $PM_{2.5}$ exposure during pregnancy, adjusting for both individual- and county-level predictors. The U.S. census division map is available at https://www.census.gov/geo/maps-data/maps/pdfs/reference/us_regdiv.pdf. SAS PROC GLIMMIX was used to implement the multilevel logistic models in this study, accounting for county level random effects. Given the narrow range of $PM_{2.5}$ exposure, we presented AORs for every 5μg/m³ increase in $PM_{2.5}$ exposure.

Finally, we conducted two sensitivity analyses. The first sensitivity analysis was to evaluate if including smoking in the models had any impact on the results from the main and stratified analyses. The second sensitivity analysis was to link U.S. EPA monitor-based $PM_{2.5}$ estimates with 2,435,805 births from 687 counties in 48 states and District of Columbia and to repeat the main and stratified analyses.

Results

Characteristics of term singleton births

Overall, there were 3,271,203 eligible term singleton infants in the contiguous US and 81,797 (3%) of them are term LBW infants in 2002 (Table 1). The proportion of term LBW infants was highest among female infants (3%), first live births (3%), births with gestational age of 37 weeks (8%), births to mothers with maternal age of <20 years (4%), non-Hispanic Black mothers (5%), unmarried mothers (4%), mothers with <12 years of education (3%), mothers with delayed or no prenatal care (3%), mothers who are smokers (5%), and mothers residing in counties with poverty rates of 20% or higher (3%), compared with their counterparts (Table 1).

$PM_{2.5}$ exposure during pregnancy

Average daily $PM_{2.5}$ exposures ranged from 4.7 to 23.8 $\mu g/m^3$ for the entire pregnancy, and from a minimum of 3.3 to a maximum of30.1$\mu g/m^3$ during individual trimesters (Table 2). Average daily $PM_{2.5}$ exposure during the entire pregnancy were strongly correlated with trimester-specific $PM_{2.5}$ exposures (correlation coefficients 0.81-0.86), but the correlations among trimester-specific $PM_{2.5}$ exposures were weaker (0.46–0.59) Table 2 shows the $PM_{2.5}$ exposure during the entire pregnancy and three trimesters for each census division. Average $PM_{2.5}$ exposure during pregnancy was generally highest (>13$\mu g/m^3$) in Middle Atlantic, East North Central, and Pacific divisions and lowest (<10 $\mu g/m^3$) in the Mountain division.

Multilevel models for the contiguous US

Associations between $PM_{2.5}$ exposure and term LBW differed for exposures averaged over the entire pregnancy and individual trimesters (Table 3). Before adjusting for covariates (Model 1), the OR for LBW in association with a 5-μg/m³ increase in $PM_{2.5}$ during the second trimester was 1.02 (95% CI: 1.00, 1.03). The OR (OR = 1.02; 95% CI: 1.01, 1.04) was similar after adjusting for county-level poverty (Model 2), but null (OR = 1.00; 95% CI: 0.99, 1.02) after additionally adjusting for individual-level predictors (Model 3).. There was a non-significant positive association between term LBW and $PM_{2.5}$ exposure during the entire pregnancy based on Model 2 (OR = 1.02; 95% CI: 0.99, 1.05) but not Model 3 (OR = 0.99; 95% CI: 0.96, 1.02). We estimated non-significant negative associations with exposure during the third trimester based on all three models (e.g., OR = 0.99; 95% CI: 0.97, 1.00 for Model 3). Analyses stratified by county poverty levels did not show consistent patterns, though LBW was significantly increased in association with $PM_{2.5}$ exposure over the entire pregnancy in counties with highest poverty rates (≥ 20%) (OR = 1.11; 95% CI: 1.00, 1.22) (see Supplemental Material, Table S1).

Multilevel models by census division

Multilevel models stratified by census division (Figure 1, Table 4) showed that, after adjusting for individual- and county-level variables, the AOR between $PM_{2.5}$ exposure and term LBW differed by census division. Significant positive associations between LBW and $PM_{2.5}$ exposure were estimated for three census divisions: the Middle Atlantic (during the entire pregnancy, OR = 1.14; 95% CI: 1.04, 1.24; and the first trimester, OR = 1.08; 95% CI: 1.03, 1.14); East North Central (during the entire pregnancy and the first and second trimesters, e.g., entire pregnancy

OR = 1.11; 95% CI: 1.04, 1.18); and West North Central divisions (second trimester OR = 1.11; 95% CI: 1.02, 1.20). There was a significant negative association between $PM_{2.5}$ exposure over the entire pregnancy and LBW in the Mountain division (OR = 0.78; 95% CI: 0.68, 0.90).

Sensitivity analyses

The analyses that adjusted smoking status yielded almost the same results (see Supplementary Material, Tables S2 and S3) as our main and stratified analyses (Tables 3 and 4), suggesting that the exclusion of maternal smoking status had little impact on the main results. The sensitivity analyses using monitor-based $PM_{2.5}$ estimates generated similar results for the main analyses, with the exception of a significant positive association for $PM_{2.5}$ over the entire pregnancy based on Model 1 (OR=1.04; 95% CI: 1.01, 1.07) (see Supplementary Material, Table S4). The sensitivity analyses using monitor-based $PM_{2.5}$ estimates also generated similar results for the stratified analyses by census division (see Supplementary Material, Table S5). Significant positive associations between LBW and $PM_{2.5}$ exposure were also estimated for two census divisions: the Middle Atlantic (the first trimester, OR = 1.06; 95% CI: 1.00, 1.11); and West North Central divisions (second trimester OR = 1.12; 95% CI: 1.01, 1.24). There was also a significant negative association between $PM_{2.5}$ exposure over the entire pregnancy and LBW in the Mountain division (OR = 0.90; 95% CI: 0.81, 1.00).

Discussion

To our knowledge, this is the first national study that linked daily $PM_{2.5}$ with individual gestational ages of term births in the contiguous US to examine the associations between term LBW and $PM_{2.5}$ exposure during the entire pregnancy as well as during specific trimesters (first,

second and third) in a multilevel framework. We used highly resolved $PM_{2.5}$ data to estimate county-level $PM_{2.5}$ exposure during pregnancy for each individual term birth for the entire population sample of pregnancies in the contiguous US in 2002. Our main national level analyses suggest no overall significant positive association between term LBW and $PM_{2.5}$ exposure during pregnancy after adjusting for known individual-level risk factors. Results from a few previous studies on $PM_{2.5}$ and term LBW drew similar conclusions (Brauer et al. 2008; Ghosh et al. 2012; Sapkota et al. 2012; Stieb et al. 2012). Our findings are also consistent with a previous study which used term births from 397 U.S. counties (Parker and Woodruff 2008). In contrast, we did not found a significant positive association between $PM_{2.5}$ and term LBW during the entire pregnancy as in a European study (Pedersen et al. 2013) and a meta-analysis of the multi-country birth data (Dadvand et al. 2013).

The results from our stratified analyses by census division showed substantial geographic variation in the associations between $PM_{2.5}$ and term LBW. There are several reasons why there may be geographic variation in the associations between $PM_{2.5}$ exposure during pregnancy and term LBW. First, this might be in part due to geographic variation in the constituents or sources of particulate matter, especially the chemical speciation of $PM_{2.5}$. Substantial geographic variations in sulfate and nitrate concentrations in $PM_{2.5}$ were observed across the US(Bell et al. 2010; Rao et al. 2003; Salam et al. 2005): very high sulfate concentration in Middle Atlantic and East North Central and East South Central; very high nitrate concentrations in East North Central and southern California; relative high nitrate concentration in Middle Atlantic and West North Central; in contrast, very low sulfate concentration in Mountain, very low nitrate in Mountain, West South Central, South Atlantic and New England. Thus, very high sulfate and/or nitrate

concentration in $PM_{2.5}$ might contribute to the positive associations between term LBW and $PM_{2.5}$ exposure during pregnancy found in Middle Atlantic and East North Central; high nitrate concentration in $PM_{2.5}$ might contribute to the positive associations found in West North Central..

Given very high nitrate and relative high sulfate concentrations in southern California, we expect a positive association between term LBW and $PM_{2.5}$ exposure during pregnancy in this area as several previous studies suggested (Basu et al. 2014; Wilhelm et al. 2012). However, our analysis using entire California term births showed consistent positive but not significant association between term LBW and $PM_{2.5}$ exposure during pregnancy (see Table 4, entire pregnancy OR=1.02, 95% CI: 0.99, 1.06; first trimester OR=1.01, 95% CI: 0.99, 1.04; second trimmest OR=1.02, 95% CI: 0.99, 1.05; third trimester OR=1.02, 95% CI:0.99, 1.06). This might be due to the difference in quantifying $PM_{2.5}$ exposure: they both used local residential census-tract-level $PM_{2.5}$ estimate, while we used more aggregated county-level $PM_{2.5}$ estimates that might have larger spatial misclassification and could impact $PM_{2.5}$ effect estimates (Ritz et al. 2007). However, Basu et al. (2004) reported that county-level metric provided a stronger association between $PM_{2.5}$ and term birth weight for a 2000 California birth cohort. This inconsistency in $PM_{2.5}$ exposure estimation makes the comparison of findings in the literature quite challenging (Basu et al. 2004).

Another explanation could be that other pollutants which co-vary with $PM_{2.5}$ are actually responsible for the apparent association between $PM_{2.5}$ and term LBW and the regional variation of that association (Bell et al. 2010; Salam et al. 2005). Also these differences could be the

result of regional differences in measurement error associated with $PM_{2.5}$ estimates. Similarly, spatiotemporal variation in weather conditions such as temperature (Wallace and Kanaroglou 2009) or humidity may contribute to the geographic variation of the association found in this study.

Lastly, regional differences in association may also reflect geographic variation in behaviors which influence exposure thus limiting the validity of using ambient $PM_{2.5}$ as a marker of exposure. A prior study, which examined the role of air conditioning on the association between particulate matter and adverse health effects among seniors residing in 168 counties found that higher prevalence of household central air conditioning was associated with lower health effect estimates for $PM_{2.5}$; air conditioning altered relationship between personal and ambient exposure (Bell et al. 2009). Our stratified analyses by trimester did not show a particularly vulnerable or sensitive $PM_{2.5}$ exposure window during pregnancy. Positive associations were found for the entire pregnancy as well as specific trimesters. Although some studies reported a stronger association in late or early pregnancy (Darrow et al. 2011), others found no particularly vulnerable or sensitive exposure window (Parker et al. 2005). Such inconsistency may partly result from spatiotemporal variation in exposure (Bell et al. 2007a) and partly reflect differences in study design (Dadvand et al. 2013).

Our analyses with both model-based and monitor-based $PM_{2.5}$ data generated similar results at national level (see Table 3 and Supplementary Material, Table S4) as well as by census division (see Table 4 and Supplementary Material, Table S5). The minor differences might reflect that the full birth sample with model-based $PM_{2.5}$ data covered all the 3,109 counties in the contiguous

US, while the birth sample with monitor-based $PM_{2.5}$ data were from only 678 counties that mainly located in highly urbanized areas. More than 94% births with monitor-based $PM_{2.5}$ data were located in central metropolitan counties (data not shown) in the contiguous US.

This study has several limitations. Foremost is the lack of data on individual maternal preexisting conditions and pregnancy complications. Maternal anemia and weight status are known risk factors for term LBW (Bodeau-Livinec et al. 2011; Han et al. 2012). Maternal obesity and underweight are both associated with birth weight and preterm birth (Han et al. 2012). A meta-analysis indicated that maternal overweight or obesity might reduce the risk of LBW but increase the risk of preterm birth (McDonald et al. 2010). Individual level residual confounding may contribute to the variation in associations between maternal exposure to ambient $PM_{2.5}$ and risk of term LBW. Also, misclassification of gestational age and imputation of date of birth are likely to affect trimester designation and exposure associated with trimesters. A related limitation is that we considered exposure during pregnancy but not earlier. For example, a mouse study of exposure (preconception and during pregnancy) to urban particulate matter suggested that both pre-gestational and gestational period exposure affected fetal weight (Veras et al. 2009). Another limitation is that we were unable to access co-exposure to noise. Traffic may affect birth weight through exposure to both air pollution and noise (Dadvand et al. 2014; Gehring et al. 2014). An additional limitation is the lack of $PM_{2.5}$ speciation data and potential measurement error due to variation of $PM_{2.5}$ within a county or during pregnancy. Furthermore, like other studies, we were unable to control for maternal mobility and indoor/outdoor activity patterns during pregnancy. Previous studies indicated 9%–32% of mothers moved during pregnancy, and over half of them moved within county (Bell and Belanger 2012; Miller et al. 2010).

Despite these limitations, this study has several strengths. Notably, our analyses were based on highly resolved $PM_{2.5}$ exposure and a full sample of eligible pregnancies in the contiguous US. Although $PM_{2.5}$ data were aggregated to county level, the daily estimates were linked to each pregnancy from imputed conception to birth days. .

This national study showed the geographic variations in the associations between $PM_{2.5}$ and term LBW in the contiguous US. The possible factors underlying these variations might include local differences in $PM_{2.5}$ exposure level and its spatiotemporal contrasts as suggested by Dadvand (Dadvand et al. 2013). Similar to this study, most previous studies of $PM_{2.5}$ and population health have focused on applying $PM_{2.5}$ mass metrics (e.g. mean, median or quartiles) to quantify the estimated effects on birth outcomes. Further studies are needed to quantify the interactions between $PM_{2.5}$ components and concentration, which may help us better understand the geographic variations in the associations between $PM_{2.5}$ and term LBW and, to some extent, explain the discrepancies in the literature. By nature, $PM_{2.5}$ is a very heterogeneous mixture of gaseous and volatile compounds and its biological toxicity might largely depend on its chemical composition (Backes et al. 2013).

In conclusion, our study provided additional evidence on the associations between $PM_{2.5}$ exposure during pregnancy and term LBW from a national perspective. We found that the magnitude and direction of estimated associations between $PM_{2.5}$ exposure and term LBW varied by geographic locations in the contiguous US. These findings may be useful to the public and policy makers in planning potential interventions to mitigate population exposure to ambient air pollution.

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Table 1. Selected characteristics of singleton term births (37– 44 weeks gestational age), US, 2002.

	Term Births		Term LBW	
Characteristics	**Number**	**Percent**	**Number**	**Percent[a]**
US (48 states and District of Columbia)	3,271,203	100	81,797	3
Infant gender				
Female	1,606,780	49	47,850	3
Male	1,664,423	51	33,947	2
Parity				
First live birth	1,320,923	40	40,219	3
Non-first live birth	1,950,280	60	41,578	2
Gestational age(weeks)				
37	312,366	10	25,193	8
38	660,074	20	22,049	3
39	930,241	28	16,222	2
40–44	1,368,522	42	18,333	1
Maternal age(years)				
Less than 20	343,361	10	13,235	4
20–34	2,489,078	76	58,262	2
35 and older	438,764	13	10,300	2
Maternal race/ethnicity				
White	1,928,006	59	39,106	2
Black	441,860	14	20,657	5
Hispanic	711,217	22	16,296	2
Other race	190,120	6	5,738	3
Marital status				
Not married	1,071,672	33	39,318	4
Married	2,199,531	67	42,479	2
Maternal education attainment(years)				
Less than 12	689,264	21	23,829	3
12	1,006,961	31	28,845	3
13–15	706,542	22	15,409	2
16 years or more	868,436	27	13,714	2
Prenatal care start time (month)				
fourth month or later/no care	509,866	16	17,603	3
first-third month	2,761,337	84	64,194	2

	Term Births		Term LBW	
Characteristics	**Number**	**Percent**	**Number**	**Percent[a]**
Smoking status				
Unknown[b]	421,172	13	8,594	2
smoker	316,727	10	17,103	5
non-smoker	2,533,304	77	56,100	2
Birth Season[c]				
Spring	808,268	25	19,740	2
Summer	850,268	26	21,178	2
Fall	828,255	25	20,819	3
Winter	784,412	24	20,060	3
County poverty rate[d]				
20% or higher	239,503	7	7,982	3
15% – 19.9%	609,592	19	17,447	3
10% – 14.9%	1,304,935	40	33,439	3
Less than 10%	1,117,173	34	22,929	2
Census Division				
New England	142,575	4	3,017	2
Middle Atlantic	413,520	13	9,972	2
East North Central	507,796	16	12,623	2
West North Central	218,318	7	4,525	2
South Atlantic	599,403	18	16,972	3
East South Central	188,987	6	5,984	3
West South Central	431,798	13	12,252	3
Mountain	250,368	8	6,230	2
Pacific	518,438	16	10,222	2

LBW, low birth weight;

[a]The percentage of term low birth weight was obtained by dividing the number of term LBW by the number of term births in the corresponding category. [b]Unknown category exclusively reflect California singleton term births – smoking status was not recorded in California birth certificate for 2002. [c]Birth season: Spring (March–May), Summer (June–August), Fall (September–November), and Winter (December–February); birth season is the only variable that was not significantly associated with term LBW. [d]The percentage of people in a county below the federal poverty line.

Table 2. County-level average daily $PM_{2.5}$ ($\mu g/m^3$) exposure during pregnancy by census division (N=3,271,203).

		Trimester		
Location	**Entire Pregnancy Mean (Min, Max), IQR**	**First Mean (Min, Max), IQR**	**Second Mean (Min, Max), IQR**	**Third Mean (Min, Max), IQR**
US (48 states and District of Columbia)	12.5 (4.7, 23.8), 4.1	12.5 (3.7, 29.6), 4.4	12.6 (3.6, 29.6), 4.4	12.6 (3.3, 30.1), 4.6
Census Division				
New England	11.8 (7.0, 14.5), 1.8	11.8 (6.2, 16.5), 2.5	11.9 (6.2, 17.4), 2.8	11.6 (5.5, 18.5), 3.2
Middle Atlantic	13.7 (7.3, 18.6), 2.5	13.6 (6.4, 24.6), 3.2	13.9 (6.4, 24.6), 3.7	13.6 (6.0, 25.2), 3.8
East North Central	13.8 (6.5, 18.1), 2.3	13.6 (5.8, 23.4), 2.8	13.7 (5.8, 25.2), 2.7	14.1 (5.6, 25.7), 3.1
West North Central	10.5 (5.7, 16.3), 2.0	10.4 (5.3, 18.1), 2.0	10.5 (5.3, 21.0), 2.2	10.7 (4.7, 21.2), 2.4
South Atlantic	12.2 (4.7, 18.1), 4.0	12.4 (3.9, 24.0), 4.0	12.2 (3.6, 23.2), 4.0	12.1 (3.3, 24.3), 4.0
East South Central	13.0 (9.3, 18.0), 2.3	13.1 (7.9, 23.2), 3.9	13.1 (7.8, 25.0), 3.7	12.9 (7.9, 25.5), 3.8
West South Central	10.8 (5.6, 15.0), 2.6	10.6 (5.2, 18.4), 3.0	10.8 (5.2, 18.4), 3.0	10.9 (4.3, 18.4), 3.1
Mountain	9.0 (5.0, 14.6), 2.6	8.9 (4.0, 25.4), 2.5	9.1 (4.1, 25.4), 2.4	9.0 (3.7, 28.4), 2.6
Pacific	14.9 (4.8, 23.8), 9.1	14.9 (3.7, 29.6), 10.1	14.8 (3.8, 29.6), 9.2	14.9 (3.9, 30.1), 8.7

N, sample size; Min, minimum; Max, maximum; IQR, interquartile range.

Table 3. Odds ratio of term LBW associated with average daily $PM_{2.5}$ exposure during pregnancy in the contiguous US[a].

Trimester	Model 1[b] (OR, 95% CI)	Model 2[c] (AOR, 95% CI)	Model 3[d] (AOR, 95% CI)
N	3,271,203	3,271,203	3,271,203
Entire Pregnancy	0.99 (0.96, 1.02)	1.02 (0.99, 1.05)	0.99 (0.96, 1.02)
First Trimester	0.99 (0.97, 1.01)	1.00 (0.98, 1.01)	1.00 (0.99, 1.02)
Second Trimester	1.02 (1.00, 1.03)*	1.02 (1.01, 1.04)*	1.00 (0.99, 1.02)
Third Trimester	0.99 (0.97, 1.00)	0.99 (0.98, 1.01)	0.99 (0.97, 1.00)

N, sample size; CI, confidence intervals; LBW, low birth weight; OR, odds ratios; AOR, adjusted odds ratios.

[a]Effect estimates (95% CI) are reported as per 5 $\mu g/m^3$ increase in $PM_{2.5}$. [b]Model 1 = $PM_{2.5}$ + county-level random effects. [c]Model 2 = Model 1 + county-level poverty. [d]Model 3 = Model 2 + individual-level covariates, including infant's gender and parity, gestational age, mother's age, race/ethnicity, marital status, education, prenatal care, birth season, and census division. * Indicates statistical significance at $p < 0.05$.

Table 4. Adjusted odds ratio of term LBW associated with average daily $PM_{2.5}$ exposure during pregnancy by census division[a].

Census Division	N	Entire Pregnancy (AOR, 95% CI)	First Trimester (AOR, 95% CI)	Second Trimester (AOR, 95% CI)	Third Trimester (AOR, 95% CI)
New England	142,575	1.00 (0.85, 1.17)	0.97 (0.86, 1.10)	1.04 (0.94, 1.15)	0.98 (0.90, 1.07)
Middle Atlantic	413,520	1.14 (1.04, 1.24)*	1.08 (1.03, 1.14)*	1.02 (0.97, 1.06)	1.04 (1.00, 1.08)
East North Central	507,796	1.11 (1.04, 1.18)*	1.07 (1.02, 1.12)*	1.06 (1.01, 1.10)*	1.02 (0.98, 1.06)
West North Central	218,318	1.08 (0.96, 1.21)	1.08 (0.97, 1.19)	1.11 (1.02, 1.20)*	0.97 (0.89, 1.05)
South Atlantic	599,403	0.97 (0.92, 1.02)	0.97 (0.93, 1.01)	1.00 (0.96, 1.03)	0.99 (0.95, 1.02)
East South Central	188,987	1.02 (0.91, 1.14)	1.00 (0.93, 1.08)	1.05 (0.98, 1.12)	0.98 (0.92, 1.05)
West South Central	431,798	0.94 (0.86, 1.02)	0.95 (0.90, 1.02)	0.98 (0.92, 1.05)	0.95 (0.89, 1.01)
Mountain	250,368	0.78 (0.68, 0.90)*	0.95 (0.90, 1.01)	0.97 (0.91, 1.02)	0.97 (0.92, 1.03)
Pacific	518,438	1.03 (1.00, 1.06)	1.02 (0.99, 1.04)	1.02 (0.99, 1.04)	1.02 (0.99, 1.05)
California	421,721	1.02 (0.99, 1.06)	1.01 (0.99, 1.04)	1.02 (0.99, 1.05)	1.02 (0.99, 1.06)

N, sample size; CI, confidence intervals; LBW, low birth weight; AOR, adjusted odds ratios.

[a]Effect estimates (95% CI) are reported as per 5 $\mu g/m^3$ increase in $PM_{2.5}$; all models include county-level random effects, $PM_{2.5}$ exposure during either entire pregnancy or a specific trimester, county-level poverty rate, and other individual-level covariates: infant's gender and parity, gestational age, mother's age, race/ethnicity, marital status, education, prenatal care, and birth season. * Indicates statistical significance at $p < 0.05$.

Figure Legends

Figure 1. Adjusted odds ratio of term LBW associated with average daily $PM_{2.5}$ exposure by census division during entire pregnancy, first trimester, second trimester, and third trimester. All models included average daily $PM_{2.5}$ exposure estimate for entire pregnancy or individual trimester, individual-level covariates: infant's gender and parity, gestational age, mother's age, race/ethnicity, marital status, education, prenatal care, birth season, and county-level poverty rate and county-level random effects.

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Figure 1.